over U.S. Patent No. 5,776,456 to Anderson et al. and other references. Claims 1, 3, 5, and 7 are also rejected under the judicially created doctrine of obviousness-type double patenting over claim 1 of U.S. Patent No. 5,776,456.

Claim 3 has been amended. Favorable reconsideration of the application based on the following amendments and remarks is respectfully requested.

Claim Objections

Claim 3 is objected to for perceived incorrect placement of a comma following the word "lymphoma." Office Action, at page 3, ¶ 1. Claim 3 has been amended in accordance with the Examiner's suggestion and to correct a spelling error.

Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

Claims 1, 3-5, and 7 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to teach methods commensurate in scope with the claims. The specification is found to be enabling for a method of treating an established CNS lymphoma. However, the Examiner contends that prophylactic measures are not taught because the specification lacks guidance on identification of those groups in need of prophylactic treatment and on safety indices of prophylactic treatment. Office Action, at pages 3-5. This rejection is respectfully traversed.

The application as originally filed specifies that the disclosed methods encompass both therapeutic and prophylactic measures. *See e.g.*, page 21, lines 23-27, and original claim 2. It is known in the art that patients that have successfully responded to treatment for CNS lymphoma are at risk of recurrence. *See e.g.*, Reni & Ferreri (2001) *Ann Hematol* 80 Suppl 3:B113-7 (copy attached). Thus, it is known that recovered CNS lymphoma patients constitute a group in need of prophylactic treatment. In addition, the safety profile of anti-CD20 antibodies has been described in numerous clinical studies. *See e.g.*, McLaughlin et al. (1998) *J Clin Oncol* 16:2825-33 (abstract attached); Piro et al. (1999) *Ann Oncol* 10:655-61 (abstract attached); Davis et al. (2000) *J Clin Oncol* 18:3135-43 (abstract attached); Davis et al. (1999) *J Clin Oncol* 17:1851-7 (abstract attached); Maloney et al. (1997) *Blood* 90:2188-95(copy attached). Thus, applicant responds that the Examiner's argument is unsupported. Specifically, a group in need of prophylactic treatment, as provided in the specification, is known in the art. Further, the non-toxicity of anti-CD20 antibodies is well-established.

Based on the foregoing, the specification is believed to be fully enabling commensurate in scope with claims 1, 3-5, and 7. Applicant respectfully requests that the rejection of claims under 35 U.S.C. § 112, first paragraph, be withdrawn. Allowance of claims 1, 3-5, and 7 is also respectfully requested.

Rejection of Claims Under 35 U.S.C. § 102(b)

Based on Maloney

Claims 1 and 7 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Maloney et al. (1997) *Blood* 90(6):2188-2195 (Maloney). In particular, the Examiner contends that Maloney teaches a method of treating low-grade or follicular non-Hodgkin's lymphoma via administration of an anti-CD20 antibody. The Examiner states that since the present specification defines a CNS lymphoma as including non-Hodgkin's lymphoma, the prior art treatment of low-grade follicular lymphoma anticipates the claims. Office Action, at pages 5-6. This rejection is respectfully traversed.

Claim 1 recites a method of treating a central nervous system (CNS) lymphoma. Applicant agrees that one type of CNS lymphoma is a non-Hodgkin's lymphoma, which is characterized as an aggressive, large cell lymphoma. *See e.g.*, Hoppe (1987) *Curr Probl Cancer* 11:363-447 (abstract attached). While Maloney discusses relapsed non-Hodgkin's lymphoma in general, the reference does not disclose any malignancies specifically associated with the CNS. That is, the recited CNS lymphoma is distinct from a low-grade or follicular non-Hodgkin's lymphoma, as described by Maloney. *Id.* Claim 1 includes the limitation of a CNS lymphoma, which is not taught or suggested by Maloney. Claim 7, which depends from claim 1, is also limited to a CNS lymphoma. Thus, applicant believes that claims 1 and 7 are patentably distinguished over Maloney and respectfully requests that the rejection of claims 1 and 7 under 35 U.S.C. § 102(b) based on Maloney be withdrawn. Allowance of claims 1 and 7 is also respectfully requested.

Rejection of Claims Under 35 U.S.C. § 103(a)

Based on Maloney and Yoneda

Claims 1, 5, and 7 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Maloney in view of U.S. Patent No. 5,626,845 (Yoneda), which describes use of Fab, Fab', and $F(ab')_2$ antibodies. The Examiner relies on Maloney as teaching a method of

treating low-grade or follicular non-Hodgkin's lymphoma via administration of an anti-CD20 antibody. The Examiner suggests that it would have been *primae facie* obvious to perform the methods of Maloney using the Fab, Fab', and F(ab')2 antibodies of Yoneda. Office Action, at pages 6-7. Applicant respectfully traverses this rejection.

As described above and incorporated herein, a CNS lymphoma is distinct from a low-grade or follicular non-Hodgkin's lymphoma, as described by Maloney. Maloney does not teach or suggest treatment of a CNS lymphoma, as recited in pending claim 1 and dependent claims 5 and 7. Maloney also does not provide any motivation for such treatment, given that management of CNS non-Hodgkin's lymphoma typically entails different methods when compared with the treatment of systemic non-Hodgkin's lymphoma, in part because many drugs do not readily traverse the blood-brain barrier. *See e.g.*, Plotkin & Batchelor (2001) *Clin Lymphoma* 1(4):263-275 (copy attached). Yoneda fails to cure the deficiencies of the primary reference. Thus, applicant submits that the present invention is not rendered obvious by the combined teachings of Maloney and Yoneda. Accordingly, applicant respectfully requests that the rejection of claims 1, 5, and 7 under 35 U.S.C. § 103(a) based on Maloney in view of Yoneda be withdrawn. Allowance of claims 1, 5, and 7 is also respectfully requested.

Rejection of Claims Under 35 U.S.C. § 103(a)
Based on U.S. Patent No. 5,776,456 and Other References

Claims 1, 3, 5, and 7 are alternatively rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent No. 5,776,456 to Anderson et al. (the '456 patent) and other references. The '456 patent is directed to methods for treating B cell lymphoma via administration of anti-CD20 in TCAE 8, ATCC Deposit No. 69119. The Examiner notes that the '456 patent does not teach treatment of CNS lymphomas, including B cell lymphomas, as now claimed. The Examiner contends that this deficiency is cured by additional references that describe most CNS lymphomas as B cell lymphomas. Office Action, at pages 10-12. This rejection is respectfully traversed.

As described above and incorporated herein, CNS lymphomas are pathologically distinct from systemic (*i.e.*, non-CNS) lymphomas and generally require distinct therapeutic approach. *See e.g.*, Hoppe (1987) *Curr Probl Cancer* 11:363-447 and Plotkin & Batchelor (2001) *Clin Lymphoma* 1(4):263-275. Methods for the treatment of systemic lymphomas are

not predictably extrapolated to treatment of CNS lymphomas with a reasonable chance of success. Accordingly, applicant respectfully requests that the rejection of claims 1, 3, 5, and 7 under 35 U.S.C. § 103(a) based on the '456 patent be withdrawn. Allowance of claims 1, 3, 5, and 7 is also respectfully requested.

Obviousness-Type Double-Patenting Rejection

Based on U.S. Patent No. 5,776,456

Claims 1, 3, 5, and 7 are also rejected under the judicially created doctrine of obviousness-type double patenting over claim 1 of U.S. Patent No. 5,776,456 (the '456 patent). Office Action, at pages 7-9. This rejection is respectfully traversed. Based on the arguments set forth above in response to the rejection of claims under § 103(a), which are incorporated herein, applicant believes that the methods of the present disclosure are non-obvious in view of the '456 patent. As such, applicant also requests that the obviousness-type double patenting rejection be withdrawn and that claims 1, 3, 5, and 7 be allowed.

Conclusion

All objections and rejections having been addressed, it is respectfully submitted that the present application is in condition for allowance and a Notice to that effect is earnestly solicited. If any points remain in issue, which the Examiner feels may be best resolved through a personal or telephone interview, he is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,

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RLT/JB/af

APPENDIX: VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

The claims were amended as indicated below. Deleted text is included in brackets ([ ]) and added text is underlined.

3. (Amended) The method of claim 1, wherein the CNS lymphoma is selected from the group consisting of: primary CNS lymphoma [,](PCNSL), leptomeningeal [metastasises] metastases (LM), or Hodgkin's disease with CNS involvement.